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10/751,235	01/02/2004	Dean DellaPenna	MSU-08604	3881

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EXAMINER
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WORLEY, CATHY KINGDON

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/751,235

Applicant(s)

DELLAPENNA ET AL.

Examiner

Cathy K. Worley

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 December 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8, 10-17 and 21-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10-17 and 21-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/27/05</u>  | 6) <input type="checkbox"/> Other: _____                                    |

DETAILED ACTION

*Restriction/Election*

1. In response to the communication received on Dec. 27, 2005 from Robert A. Goetz, the election without traverse of group I, claims 1-17 and 21-32 as they relate to SEQ ID NO:5, is acknowledged. The cancellation of claims 9 and 18-20 is acknowledged. The Applicant is reminded that, as stated in the restriction requirement mailed on Nov. 3, 2005, the election of a sequence for examination is NOT an election of species, and therefore the non-elected sequences are withdrawn from consideration. The Applicant was directed to choose one sequence and, instead chose two sequences, SEQ ID NO:5 and NO:4. The Examiner spoke with Lisa Austin on Mar. 6 to get clarification on the relationship between the different sequences, and because SEQ ID NO:4 is encoded by SEQ ID NO:5, it is proper to keep these sequences together. In addition, Lisa Austin explained that SEQ ID NO:1 is a subsequence of SEQ ID NO:4 and, therefore, is encoded by SEQ ID NO:5, so claims directed to SEQ ID NO:1 will also be examined. The Examiner thanks Lisa Austin for the helpful clarification by phone.

Lisa Austin explained that each of the proteins encoded by the different sequences recited in claim 10 comprise a polypeptide domain that is at least 40% identical to SEQ ID NO:1 as recited in claim 1. This makes claims 1-8, 10-17, and 21-32 linking claims that link the individual sequences recited in claim 10. The restriction requirement between the linked inventions (the individual sequences

recited in claim 10) is subject to the nonallowance of the linking claims. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant applications. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP 804.01.

Claims 1-8, 10-17, and 21-32 are pending. Applicant is advised to amend the claims to read only on the elected sequence. The restriction requirement is made FINAL.

### *Specification*

2. The specification is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. On page 43 in line 1, page 46 in line 19, page 48 in line 7, page 98 in lines 11 and 30, page 99 in lines 20 and 25-27, page 102 line 25, and page 104 in line 12 there are embedded links. Applicant is

required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP 608.01.

3. The abstract of the disclosure is objected to because it is not descriptive enough of the elected invention. Applicant is advised to amend the abstract to include the organism from which the gene has been taken. The abstract should be between 50-150 words in length and be descriptive of the elected invention. It is currently 40 words long and does not disclose the organism from which LUT1 was taken. Correction is required. See MPEP § 608.01(b).

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: - - LUT1 gene from Arabidopsis and its use in engineering carotenoid metabolism in plants - - .

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5-8, 13, and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-8 recite sequence, polypeptide, or motif "corresponding" to an identified sequence. The use of the word "corresponding" renders these claims indefinite. What is meant by "corresponding"? Does this mean the sequence, polypeptide, or motif consists of the identified sequence? Does this mean the sequence, polypeptide, or motif comprises the identified sequence? Does this mean the sequence, polypeptide, or motif is related to the identified sequence by homology or derived from the identified sequence in some way? These claims, as written, do not sufficiently define the metes and bounds of the invention.

Claim 13 is indefinite because it is unclear what is meant by "plant vector comprises a T-DNA vector". Does this mean there are two vectors fused together?

Claims 16-17 recite the limitation "said promoter" in line 1. There is insufficient antecedent basis for this limitation in the claims because they depend from claim 15 which is drawn to a nucleic acid sequence encoding a polypeptide; not to a promoter.

6. Claims 1-8, 11-17, and 21-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. All dependent claims are included in the rejection.

Claims 1, 15, 21, and 25-31 recite “a nucleic acid sequence encoding a polypeptide at least 40% identical to SEQ ID NO:1” in conjunction with specified enzyme activities. SEQ ID NO:1 identifies a polypeptide consisting of 77 amino acid residues, therefore a polypeptide that is at least 40% identical to SEQ ID NO:1 can have 46 amino acid substitutions. Given that there are 20 different amino acids, the genus of molecules that can have any amino acid residue at 46 different positions within the polypeptide encompasses  $20^{46}$  molecules which is  $7 \times 10^{59}$  molecules. Furthermore, each of these multitudes of polypeptides can be encoded by any nucleic acid molecule having the necessary codons, so the genus of nucleic acid molecules encompassed by these claims is even larger than the genus of polypeptides. There was only one nucleic acid molecule (SEQ ID NO:5) shown to have functional activity by complementing a mutant phenotype in Arabidopsis (see pages 101-102, Example 3, in particular). Given the multitudes of molecules encompassed by the claims and only one shown to have any functional activity, this is not a representative number of species for the large genus being claimed.

The specification speculates that the enzymatic activity encoded by SEQ ID NO:5 is  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity from a cytochrome P450 monooxygenase (see page 102 lines 3-5, pages 103-104 Example 5, and page 101

lines 3-5, in particular). The specification describes motifs/domains that are known in the art to correspond to an oxygen binding pocket, SEQ ID NO:12, a transmembrane domain, SEQ ID NO:10, a cysteine/heme-binding motif, SEQ ID NO:14, and a chloroplast targeting peptide, SEQ ID NO:11 (see pages 102-103, in particular), but there are no working examples where these activities are proven. The only proven functional activity is the ability of SEQ ID NO:4 or 5 to complement the *lut1* mutation in Arabidopsis. However, the specification does not describe any specific structural features that correspond to the functional activity of being able to complement the *lut1* mutation.

Given the large genus of molecules encompassed by the claims, and given the lack of description of structural features corresponding to function, the written description requirements have not been met.

7. Claims 1-8, 10-15, and 21-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-8, 10-15, and 21-32 are broadly drawn to expression vectors, nucleic acids, transgenic plants and seeds, and methods comprising a nucleic acid sequence



encoding a polypeptide at least 40% identical to SEQ ID NO:1 and having specified enzymatic activities.

The nature of the invention is molecular biological approaches for using a nucleic acid discovered by complementing a mutant.

The specification discloses that a nucleic acid comprising SEQ ID NO:5 was identified by its ability to complement the *lut1* mutation in Arabidopsis (see page 102 lines 6-9 and Figure 19a, in particular). This nucleic acid encodes the amino acids identified as SEQ ID NO:4 (see Figure 19a, in particular). A subsequence of SEQ ID NO:4 is identified as SEQ ID NO:1 (see Figure 18, in particular). The specification discloses that bioinformatics analyses suggests the polypeptide of SEQ ID NO:4 is a cytochrome P450 enzyme and comprises an oxygen binding pocket consensus sequence (SEQ ID NO:12), a heme-binding cysteine motif (SEQ ID NO:14), a chloroplast targeting peptide (SEQ ID NO:11), and a transmembrane domain (SEQ ID NO:10), (see pages 102-103 and Figure 22, in particular).

The specification does not disclose any enzyme assays showing that the protein encoded by SEQ ID NO:5 has a specific enzymatic function. Transformation of the *lut1* mutant Arabidopsis plant with SEQ ID NO:5 complements the mutant phenotype and therefore, either directly or indirectly, provides  $\epsilon$ -ring hydroxylase and  $\beta$ -ring hydroxylase activity (see page 103-104 and Figure 17, in particular). Furthermore, subsequent experimental work was unsuccessful in providing an assay for enzymatic function (see Tian et al. PNAS (2004) Vol. 101, pp. 402-407).

Tian et al. teach that initial attempts to express and assay LUT1 protein in yeast were unsuccessful (see Tian et al., page 405, left column, in particular), and expression in bacteria is highly unlikely to work given the problems of expression eukaryotic membrane proteins in prokaryotic systems (see Hannig et al. TIBTECH (1998) Vol. 16, "focus", see second-to-last page, right column, in particular).

Therefore, one of skill in the art would not know how to use the nucleic acids and vectors for prokaryotic or yeast expression (claims 11 and 14 are specifically not enabled for these reasons).

The instant application speculates that SEQ ID NO:5 encodes a cytochrome P450 enzyme with  $\epsilon$ -ring hydroxylase and  $\beta$ -ring hydroxylase activity that is involved in carotenoid biosynthesis, however, even if this hypothesis is true, multiple enzymes are involved in this pathway, and it is highly unpredictable what phenotype would result from overexpression of only one of the enzymes involved. The prior art teaches that metabolic engineering of biosynthetic pathways is highly unpredictable (see Stephanopoulos et al. TIBTECH (1993), Vol. 11, pp. 392-396). It is possible the required enzymes may have to be present in stoichiometric quantities, or there could be feedback regulation mechanisms that are complex. It would require undue experimentation on the part of one of skill in the art to determine the results of expressing SEQ ID NO:5 in a plant, and to elucidate what other steps (if any) would be required to generate a useful plant. Given this unpredictability and given that the specification in the instant application has not

provided any working examples of expression of SEQ ID NO:5 in a healthy wild-type plant to demonstrate there is an effect on carotenoid metabolism (other than complementing a mutant which is deficient in the identical enzyme), one of skill in the art would not know how to use the claimed expression vectors, nucleic acids, transgenic plants and seeds, and the methods recited in claims 28-32 are not enabled.

Even if the Applicant can provide support for a use of SEQ ID NO:5, the enablement would not be extended to the entire genus of molecules encompassed by these claims. The claims encompass nucleic acids encoding polypeptides with as little as 40% identity to SEQ ID NO:1, and one of skill in the art would not know how to use any such nucleic acids. The specification does not disclose any nucleic acid other than SEQ ID NO:5 that encodes a polypeptide at least 40% identical to SEQ ID NO:1, and there are multitudes of nucleic acids encompassed by this recitation as discussed above in the written description rejection. Even if there were some guidance on how to use a nucleic acid encoding  $\epsilon$ -ring hydroxylase and  $\beta$ -ring hydroxylase activity that is involved in carotenoid biosynthesis, there is no guarantee that a polypeptide with as little as 40% identity to SEQ ID NO:1 would have such activity. The polypeptide comprising SEQ ID NO:1 has not been shown to have any activity other than the expression of the entire protein of SEQ ID NO:4 which has the function of complementing the *lut1* mutant phenotype in Arabidopsis. The specification has not provided any working example to demonstrate that a

polypeptide comprising SEQ ID NO:1, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and SEQ ID NO:14 would be capable of catalyzing any reaction at all. These domains, put together, have not been shown to be sufficient for enzymatic activity or the desired carotenoid biosynthesis function.

Given the breadth of the claims, the unpredictability in the art, and the lack of working examples, it would require undue experimentation on the part of one of skill in the art to make and use the invention as claimed.

*Claim Rejections - 35 USC § 102*

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-8, 11-17, 21-22, and 24-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Kovalic (US Patent Application Pre-Grant Publication US 2004/0216190 A1, published on Oct. 28, 2004; filed on Dec. 18, 2003).

Claims 1-8, 11-17, 21-22, and 24-28 are drawn to expression vectors, transgenic plants and seeds, and methods comprising a nucleic acid sequence encoding a polypeptide at least 40% identical to SEQ ID NO:1 and having specified enzymatic activities.

Kovalic teaches a nucleic acid which is 32.5% identical to SEQ ID NO:5, and which encodes a protein comprising polypeptides that are 100% identical to SEQ ID NOs: 1, 10, 11, 12, and 14 (see STIC Sequence search results). If the property of having monooxygenase P450 activity or  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity is an inherent property of the polypeptides encompassed by these claims, then the polypeptide encoded by the nucleic acid taught by Kovalic has monooxygenase P450 activity or  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity. This satisfies the limitations of claims 1-8 of the instant application. If the polypeptide encoded by the nucleic acid taught by Kovalic does not have monooxygenase P450 activity or  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity, then the claims of the instant application have not included enough structural limitations to distinguish from the prior art, and the specification of the instant application has not provided sufficient description of the structures required for these activities.

Kovalic teaches eukaryotic and prokaryotic vectors (see paragraph 0066, in particular), and plant expression vectors, including T-DNA vectors (see paragraph 0076, in particular), which satisfies the limitations in claims 11-14 of the instant application. Kovalic teaches constructs comprising promoters that direct transcription of the protein-encoding region and several plant promoters (see paragraph 0069, in particular), which satisfies the limitations of claims 15-17 of the instant application. Kovalic teaches plants transformed with these constructs

including tobacco which is a solanaceae (see paragraph 0021, in particular) which satisfies the limitations of claims 21-22 and 24-27 of the instant application.

Kovalic teaches methods of generating transgenic plants comprising these DNA constructs (see paragraphs 0021 and 0067, in particular), which satisfies the limitations of claims 28-32 of the instant application.

9. Claims 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Comai et al. (US Patent # 5,187,267, issued on Feb. 16, 1993).

Claims 16 and 17 are drawn to a eukaryotic promoter and a promoter that is active in a plant. Because these claims lack antecedent basis (see 112 2<sup>nd</sup> rejections above), the limitations from the parent claim are not included.

Comai teaches a eukaryotic promoter that is active in a plant that was derived from the tomato heat shock protein, hsp80, (see claim 1).

10. Claims 1-8 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyakatura et al. (GenBank Accession AL132958, published on Dec. 21, 1999), see STIC sequence search report.

Claims 1-8 and 10-12 are drawn to an expression vector.

Nyakatura et al. teach a BAC clone that contains the genomic sequence comprising SEQ ID NO:5 of the instant application (see STIC sequence search). This BAC clone could be used as an expression vector wherein expression of the

protein encoded by SEQ ID NO:5 is regulated by its own native promoter. Because this clone comprises SEQ ID NO:5, it encodes all the domains recited in claims 5-8 and it inherently has the activities recited in claims 1-4.

11. Claims 1, 5, 7, 11-13, 21-22, 24-26, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Siminszky et al. (US Patent No. 6,121,512, issued on Sept. 19, 2000).

Claims 1, 5, 7, 11-13, 21-22, 24-26, and 28 are drawn to expression vectors, transgenic plants and seeds, and methods comprising a nucleic acid sequence encoding a polypeptide at least 40% identical to SEQ ID NO:1 and having monooxygenase P450 activity.

Siminszky et al. teach a nucleic acid encoding a cytochrome P450 with 50.89% identity to SEQ ID NO:1 in the instant application (see STIC sequence search results). Siminsky et al teach that the cDNAs encode P450 consensus sequences (see column 15, in particular) which satisfies the limitations in claims 5 and 7 in the instant application. Siminszky et al. teach expression cassettes comprising said nucleic acid and transformation of plants with said expression cassettes, and the use of the Agrobacterium Ti plasmid (see columns 5 and 6, and column 9, in particular) which satisfies the limitations of claims 11-13, 21, 25, and 28 in the instant application. Siminszky et al. teach the transformation of many kinds of plants including brassicaceae (see column 10, in particular) and crop plants

(see column 11, in particular) which satisfies the limitations of claims 22 and 24 in the instant application. Siminszky et al teach transformed plant seeds (see column 11, in particular) which satisfies the limitations of claim 26 in the instant application.

12. Claims 1, 11-12, 21-22, 24-26, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Bloksberg et al. (US Patent No. 6,410,718 B1, issued on June 25, 2002).

Claims 1, 11-12, 21-22, 24-26, and 28 are drawn to expression vectors, transgenic plants and seeds, and methods comprising a nucleic acid sequence encoding a polypeptide at least 40% identical to SEQ ID NO:1 and having monooxygenase P450 activity.

Bloksberg et al. teach a nucleic acid encoding a polypeptide with 49.87% identity to SEQ ID NO:1 in the instant application (see STIC sequence search results). Bloksberg et al. teaches expression cassettes comprising said nucleic acid (see column 19, in particular). Bloksberg et al. teach the use of eukaryotic plant promoters (see column 22, in particular) which satisfies the limitations of claims 11 and 12 in the instant application. Bloksberg et al. teach transgenic plants, including tobacco (which is a Solanaceae) and corn (which is a crop plant), and they also teach seeds of said plants (see column 22, in particular), which satisfies the limitations of claims 21-22 and 24-26. Bloksberg et al. teach the transformation of



these plants (see paragraph bridging columns 21 and 22, in particular) which satisfies the limitations of claim 28.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 1-8, 10-13, 15-17, 21-22, and 24-32 are rejected under 35

U.S.C. 103(a) as being unpatentable over Siminszky et al. (US Patent No. 6,121,512, issued on Sept. 19, 2000) as applied to claims 1, 5, 7, 11-13, 21-22, 24-26, and 28 above, in view of Nyakatura et al. (GenBank Accession AL132958, published on Dec. 21, 1999), and further in view of Ohkawa et al. (Pesticide Science (1999), Vol. 55, pp. 867-874).

Claims 1-8, 10-13, 15-17, 21-22, and 24-32 are drawn to expression vectors, transgenic plants and seeds, and methods comprising a nucleic acid sequence encoding a polypeptide at least 40% identical to SEQ ID NO:1 and having monooxygenase P450 activity.

Siminszky et al. teach expression vectors, transgenic plants and seeds, and methods comprising a nucleic acid sequence encoding a polypeptide at least 40%

identical to SEQ ID NO:1 and having monooxygenase P450 activity, as discussed above in the 102(b) rejection.

Siminszky et al. do not teach a nucleic acid encoding a polypeptide with  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity, nor do they teach SEQ ID NO:10, SEQ ID NO:11, or SEQ ID NO:5.

Nyakatura et al. teach the entire sequence of SEQ ID NO:5 which encodes a polypeptide with  $\epsilon$ -ring hydroxylase or  $\beta$ -ring hydroxylase activity, and this polypeptide comprises SEQ ID NO:10 and SEQ ID NO:11, as discussed above in the 102(b) rejection.

At the time the invention was made, it would have been obvious and within the scope of one of skill in the art to modify the methods taught by Siminsky et al. to utilize a nucleic acid comprising SEQ ID NO:5 as taught by Nyakatura et al. One would have been motivated to do so because Ohkawa et al. teach that many cytochrome P450s can be useful as herbicide resistance genes in transgenic plants, and it is difficult to identify which specific P450 species can be used, therefore, it is useful to transform plants with multiple P450 genes (see page 870, in particular). Because Nyakatura clearly identify a region of their BAC clone as being a P450 gene, it would have been obvious to utilize this region in the method taught by Siminsky et al.

14. Claim 23 is free of the prior art because the prior art does not teach or fairly suggest the transformation of a marigold with the recited nucleic acid construct.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CKW  
Mar. 16, 2006

MEDINA A. IBRAHIM  
PRIMARY EXAMINER

*Medina A. Ibrahim*